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Benefits versus risks of using albumin in critically ill patients

An Essay
Submitted for partial fulfillment of master degree in intensive care

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Abbrev	*Full term*
ALT	Alanine aminotransferase
aPTT	Activated partial thromboplastin time
ARDS	Acute respiratory distress syndrome
AST	Aspartate aminotransferase
BP	Blood pressure
Ca^{2+}	Calcium
CBF	Cerebral blood flow
CO	Cardiac output
CO_2	Carbon dioxide
COP	Colloid oncotic pressure
CVP	Central venous pressure
Cys.	Cysteine
D	Dalton
E_2	Estradiol
ECF	Extracellular fluid
FFP	Fresh frozen plasma
GFR	Glomerular filtration rate
GI	Gastrointestinal
HA	Human Albumin
HAS	Human Albumin solution
HB	Haemoglobin
HES	Hydroxyethyl starch
HRS	Hepatorenal syndrome
IC	Immunocomplexes
ICAM	Intra-cellular adhesion molecule
ICS	Intracellular space
ICU	Intensive care unit

IL-6	Interleukin 6
IMA	Ischaemic modified albumin
INR	International normalized ratio
ISS	Interstitial space
IV	Intravenous
IVS	Intravascular space
JVP	Jugular venous pressure
K^+	Potassium
KDa	Kilo Dalton
Lys.	Lysine
MAP	Mean arterial pressure
MARS	Molecular adsorbant reticulating system
MELD	Model for end stage liver disease
Mg^{2+}	Magnesium
MODS	Multiple organ dysfunction syndrome
MOF	Multiple organ failure
MW	Molecular weight
Na^+	Sodium
NO	Nitric oxide
NS	Normal Saline
OHSS	Ovarian hyperstimulation syndrome
PAWP	Pulmonary artery wedge pressure
PCCO	Pulse contour cardiac output
PMNs	Polymorphonuclear cells
PN	Parentral nutrition
PPCD	Post-paracentesis circulatory dysfunction
PR	Pulse rate
PRBCs	Packed red blood cells
PTT	Partial thromboplastin time

RBCs	Red blood cells
RL	Ringer Lactate
SAFE	Saline versus Albumin fluid evaluation
SAH	Subarachnoid haemorrhage
SBP	Spontaneous bacterial peritonitis
SIRS	Systemic inflammatory response syndrome
SLE	Systemic lupus erythematosus
T_4	Tetra iodo thyronine
TBSA	Total body surface area
TEG	Thromboelastogram
TER	Transcapillary escape rate
TNF-α	Tumor necrosis factor- α
TPN	Total parentral nutrition
TRICC	Transfusion requirements in critical care
vWF	Von willebrand factor

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Introduction

Fluid resuscitation remains one of the most common therapeutic interventions performed on acutely ill patients in the intensive care unit. Despite this, the optimal type of fluid (crystalloid or colloid) employed, and its constituents, have been a source of controversy in the medical literature for many years. Human albumin administration has often been at the heart of this debate **(*Peters, 2006*)**.

Albumin is the predominant product of hepatic protein synthesis and one of the more abundant plasma proteins. Albumin comprises 75-80% of normal plasma colloid oncotic pressure and 50% of protein content **(*Peters, 2006*)**.

Among its multiple physiologic roles, it plays an essential part in the generation of colloid-oncotic pressure. Also, albumin transports various substances, including bilirubin, fatty acids, metals, ions, hormones, and exogenous drugs, in addition to its metabolic role in acid-base balance, as an antioxidant and as an anticoagulant **(*Schierhout and Roberts, 2005)***.

Albumin`s limited availability and high cost make it essential to define recommendations for its appropriate use, as an alternative to other therapeutic strategies including solutions of crystalloids and non-protein colloids, and have also stimulated numerous studies, which have sometimes reached contradictory conclusions **(*Schierhout and Roberts, 2005)***.

Aim of the work

The aim of this work is to highlight the appropriate use of albumin in critically ill patients as regards its benefits and risks.

Colloid and Crystalloid Resuscitation

Hypovolaemia is one of the most common and potentially reversible crises in acute medicine. It occurs as the result of fluid loss (e.g. bleeding, burns, vomiting and diarrhoea) or vasodilatation of the circulating volume (e.g. septic shock). In either case, rapid correction is mandatory. In the setting of intensive care, there is the initial challenge of shock and resuscitation but there is also the often overlooked challenge of maintaining euvolaemia ***(Hillman et al., 2005)***.

The debate about whether to use crystalloids or colloids for the resuscitation of hypovolaemia is not as important as the challenge of continually maintaining a normal intravascular volume ***(Hillman et al., 2005)***.

In the daily routine of intensive care hypovolaemia is continually monitored with vital signs such as blood pressure (BP) and pulse rate (PR) as well as by monitoring end organ function such as urine output and peripheral perfusion. Even minor degrees of hypovolaemia can cause ischaemia and organ dysfunction (***Sakka et al., 2007)***.

Therefore, the first signs of hypovolaemia should be expected, and on detecting it, any deficit should be corrected rapidly. The usual strategy in the Intensive Care Unit (ICU) is either to increase the rate of intravenous (IV) fluid infusion or deliver a bolus of 1-2 L (20 ml/kg in a pediatric patient) as a fluid challenge and then the effect is assessed and the fluid rate is adjusted accordingly ***(Reinhart et al.,2012).***

The importance of maintaining the intravascular space (IVS) is related to the deleterious effects of ischaemia. There is no conclusive data on exactly how much ischaemia can be safely tolerated. Particularly important are cells with high metabolic rates such as the brain, heart and kidney. These organs initially have their blood supply protected by auto-regulation at the expense of decreased blood supply to non-vital organs such as the skin and muscle. Ischaemia can be better tolerated in organs such as the skin or muscle as they have a low metabolic rate. However, there comes a point when even these cells begin to malfunction. Even minor degrees of hypovolaemia predisposes to splanchnic hypoperfusion, predisposing to translocation of bacteria and

bacterial breakdown products. This can in turn predispose to multiorgan dysfunction syndrome (MODS) and even death as shown in figure (1) ***(Sakka et al., 2007).***

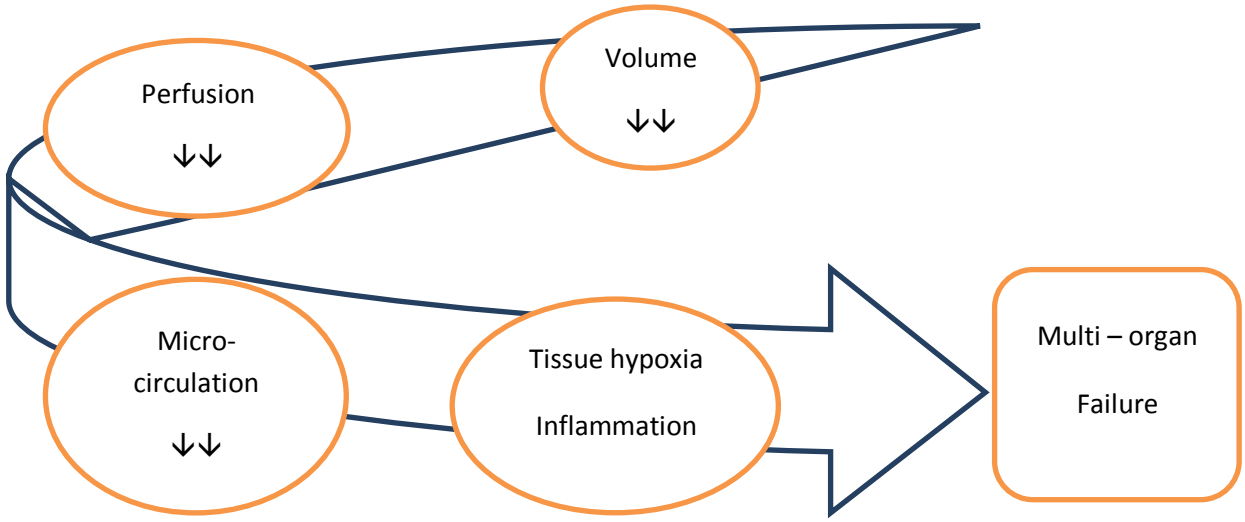

Figure (1): Effect of ischaemia on different body organs *(Sakka et al., 2007)*.

Cytokines are also released as a result of the ischaemia itself, adding to the multiorgan dysfunction syndrome (MODS) ***(Biffland, 2006).***

The concept of early detection and correction of ischaemia, as well as rapid establishment of an airway and delivery of adequate oxygen delivery is the basis of the 'Golden Hour', emphasizing the importance of rapid resuscitation in order to prevent cellular damage. The so-called 'Golden Hour' applies not only to initial resuscitation but also to continually maintaining the IVS, while the patient is in the intensive care unit ***(Boldt, 2008).***

There is no proven place for deliberately tolerating even the smallest degree of ischaemia. While deliberate hypoventilation or permissive hypercarbia is a proven strategy to protect overventilation of lungs and damage to alveoli; permissive hypercarbia does not mean permissive hypoxia. And permissive hypercarbia and its benefits do not equate to permissive hypotension, which in fact is "permissive shock and ischaemia" as in table (1). In special circumstances such as penetrating injury, it

may be better to perform definitive surgery rapidly rather than attempt to restore circulating volume **(*Boldt, 2008).***

Table (1): Goals for fluid resuscitation

- Achievement of normovolaemia and haemodynamic stability.
- Correction of major acid-base disturbances.
- Compensation of fluxes from the interstitial/intracellular compartments.
- Improvements of microvascular blood flow.
- Prevention of activation of inflammatory cascade system
- Normalization of oxygen delivery to tissue cells and cell metabolism.
- Prevention of reperfusion injury.

(Boldt, 2008).

The Body's Fluid Space

There are approximately 40 L of water in a 70 kg adult male - 60% of the body's weight. In the newborn it is closer to 80% and in the very old, approximately 40%. In other words, the young requires higher maintenance fluid and as you age, you contain less water. The water is distributed between three spaces, each with a distinct function and set of physiological principles governing its volume - the intravascular space (IVS); the interstitial space (ISS); and the intracellular space (ICS) ***(Sakka et al., 2007)***.

Intravascular Space

The intravascular space (IVS) contains about 5 L of blood - red cells and plasma. The circulation delivers nutrients and oxygen to cells and removes carbon dioxide and products of metabolism. The IVS is contained within the circulation by the endothelial cells which, while allowing some leakage of large molecules such as proteins, largely encourages their retention within the IVS, generating a colloid oncotic pressure (COP), which encourages fluid movement from the interstitial space (ISS), counteracting the